SNCA gene

synuclein alpha

Normal Function

The *SNCA* gene provides instructions for making a small protein called alpha-synuclein. Alpha-synuclein is abundant in the brain, and smaller amounts are found in the heart, muscles, and other tissues. In the brain, alpha-synuclein is found mainly at the tips of nerve cells (neurons) in specialized structures called presynaptic terminals. Within these structures, alpha-synuclein interacts with fats (lipids) and proteins. Presynaptic terminals release chemical messengers, called neurotransmitters, from compartments known as synaptic vesicles. The release of neurotransmitters relays signals between neurons and is critical for normal brain function.

Although the function of alpha-synuclein is not well understood, studies suggest that it plays an important role in maintaining an adequate supply of synaptic vesicles in presynaptic terminals. It may also help regulate the release of dopamine, a neurotransmitter that is critical for controlling the start and stop of voluntary and involuntary movements.

Health Conditions Related to Genetic Changes

multiple system atrophy

Several common variations in the *SNCA* gene have been found to increase the risk of multiple system atrophy, a progressive brain disorder that affects movement and balance and disrupts the function of the autonomic nervous system. The autonomic nervous system controls actions that are mostly involuntary, such as regulation of blood pressure.

The identified gene variations each change a single DNA building block (nucleotide) in the *SNCA* gene. Researchers are working to determine whether these changes alter the function of alpha-synuclein and how they influence the risk of developing multiple system atrophy. Variations in the *SNCA* gene appear to affect disease risk in people of European descent; studies suggest that changes in this gene are not associated with multiple system atrophy in the Chinese population or in South Koreans. It is unclear whether *SNCA* gene variations are a risk factor for this condition in people of other geographic and ethnic backgrounds.

Parkinson disease

At least five mutations in the *SNCA* gene have been found to cause Parkinson disease, a condition characterized by progressive problems with movement and

balance. *SNCA* gene mutations are associated with the early-onset form of the disorder, which typically appears before age 50. Other variations in the *SNCA* gene have been found to increase the risk of developing Parkinson disease, although they do not appear to be a direct cause of the disease.

Researchers have described two types of alterations of the *SNCA* gene in people with Parkinson disease. One type changes a single protein building block (amino acid) used to make alpha-synuclein. In some cases, the amino acid alanine is replaced with the amino acid threonine at protein position 53 (written as Ala53Thr or A53T) or with the amino acid proline at position 30 (written as Ala30Pro or A30P). These mutations cause the alpha-synuclein protein to take on an incorrect 3-dimensional shape (misfold). In the other type of alteration, one of the two *SNCA* genes in each cell is inappropriately duplicated or triplicated. The extra copies of the *SNCA* gene lead to an excess of alpha-synuclein.

It is unclear how alterations in the *SNCA* gene cause Parkinson disease. This condition involves the selective death or impairment of neurons that produce dopamine. Misfolded or excess alpha-synuclein proteins may cluster together (aggregate) and impair the function of these neurons in specific regions of the brain. Aggregated alpha-synuclein may disrupt the regulation of dopamine, which allows dopamine to accumulate to toxic levels and eventually kill neurons. Researchers also suspect that misfolded or excess alpha-synuclein stalls or shuts down the cell machinery that removes unneeded proteins. As a result, unneeded proteins may clog neurons and impair their functions. Symptoms of Parkinson disease appear when dopamine-producing neurons become impaired or die. The loss of these cells weakens communication between the brain and muscles, and ultimately the brain becomes unable to control muscle movement.

Misfolded alpha-synuclein is also a major component of Lewy bodies, which are abnormal deposits that appear in certain neurons in the brain in people with Parkinson disease. The presence of Lewy bodies in a region of the brain called the substantia nigra, which controls balance and movement, are a characteristic feature of Parkinson disease. However, it is unclear whether Lewy bodies play a role in killing nerve cells or if they are part of the cells' response to the disease.

other disorders

Researchers have identified mutations in the *SNCA* gene that may lead to a loss of intellectual functions (dementia). Several mutations cause a disorder known as Lewy body dementia, in which dementia is associated with deposits of Lewy bodies in certain areas of the brain. Although the features of this disorder are variable, symptoms typically include dementia, visual hallucinations, fluctuations in attention, and changes characteristic of Parkinson disease (described above) such as trembling or rigidity of limbs, slow movement, and impaired balance and coordination. Lewy

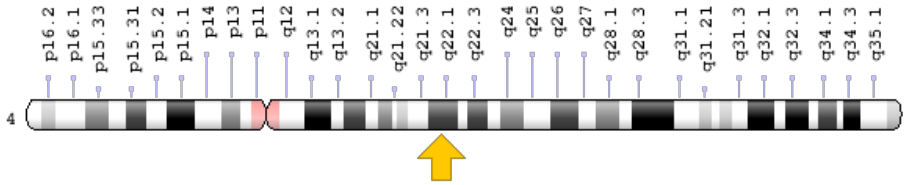
bodies are also a feature of Parkinson disease, but these abnormal deposits tend to be more widespread in the brain in Lewy body dementia.

One of the *SNCA* mutations responsible for Lewy body dementia replaces the amino acid glutamic acid with the amino acid lysine at position 46 in the alpha-synuclein protein (written as Glu46Lys or E46K). Another mutation replaces the amino acid alanine with the amino acid threonine at position 53 (written as Ala53Thr or A53T). Both of these mutations have also been found in people with Parkinson disease.

Chromosomal Location

Cytogenetic Location: 4q22.1, which is the long (q) arm of chromosome 4 at position 22.1

Molecular Location: base pairs 89,724,099 to 89,838,324 on chromosome 4 (Homo sapiens Annotation Release 108, GRCh38.p7) (NCBI)



Credit: Genome Decoration Page/NCBI

Other Names for This Gene

- alpha-synuclein
- NACP
- nonA-beta component of AD amyloid
- PARK1
- PARK4
- PD1
- synuclein, alpha (non A4 component of amyloid precursor)
- SYUA_HUMAN

Additional Information & Resources

Educational Resources

- Basic Neurochemistry (sixth edition, 1999): Composition of Synaptic Vesicles
  https://www.ncbi.nlm.nih.gov/books/NBK28154/
- Madame Curie Bioscience Database: α-Synuclein Physiology and Membrane Binding
  https://www.ncbi.nlm.nih.gov/books/NBK6143/
- National Institute of Neurological Disorders and Stroke: Dementia with Lewy Bodies
  https://www.ninds.nih.gov/Disorders/All-Disorders/Dementia-Lewy-Bodies-Information-Page

GeneReviews

- Parkinson Disease Overview
  https://www.ncbi.nlm.nih.gov/books/NBK1223

Genetic Testing Registry

- GTR: Genetic tests for SNCA
  https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=6622%5Bgeneid%5D

Scientific articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28SNCA%5BTIAB%5D%29+OR+%28alpha-synuclein%5BTIAB%5D%29%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+360+days%22%5Bdp%5D

OMIM

- DEMENTIA, LEWY BODY
  http://omim.org/entry/127750
- SYNUCLEIN, ALPHA
  http://omim.org/entry/163890

Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology
  http://atlasgeneticsoncology.org/Genes/GC_SNCA.html
- ClinVar
  https://www.ncbi.nlm.nih.gov/clinvar?term=SNCA%5Bgene%5D

- HGNC Gene Family: Parkinson disease associated genes
  http://www.genenames.org/cgi-bin/genefamilies/set/672
- HGNC Gene Symbol Report
  http://www.genenames.org/cgi-bin/gene_symbol_report?q=data/hgnc_data.php&hgnc_id=11138
- NCBI Gene
  https://www.ncbi.nlm.nih.gov/gene/6622
- PDGene
  http://www.pdgene.org/view?gene=SNCA
- UniProt
  http://www.uniprot.org/uniprot/P37840

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